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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/713,578	AWASTHI ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *9-46 and 48-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Reside Def. and iHOP database*.

DETAILED ACTION

Election/Restrictions

The Election filed on October 17, 2005 in response to the Restriction Requirement of 09/22/2005 has been entered. Applicant's election of Group I, claims 1-8 and 47, as as specifically drawn to a method of preparing a proteoliposome comprising the steps of contacting a liposome with an effective portion of RLIP76 to create a proteoliposome, further comprising adding the proteoliposome to a toxic compound, wherein the toxic compound resides in an organism, mammalian cell or transfected mammalian cell has been acknowledged.

Applicant's election with traverse of Group I, Claims 1-8 and 47, is acknowledged. The traversal is on the grounds that a thorough search of the subject matter of Claims 9-46, 48-52 and the non-elected subject matter of Claim 4 would necessarily include a search of similar subject matter because all of the claims are drawn to a proteoliposome comprising a liposome and an effective portion of RLIP76. For example, Applicants submit that any art identified within Group I would necessarily include art identified Group II and VI. Moreover, Applicants submit that all the methods require contact of a liposome and an effective portion of RLIP76. Accordingly, Applicants assert that, as claimed, the processes of making are not materially distinct from the product made because the processes as claimed do not make a materially different product. As such, Applicants contend that the inventions are not distinct and do not have separate status in the art. Furthermore, Applicant's submit that the Examiner has not materially shown the inventions to be distinct, e.g., by showing the different classification of each group.

These arguments have been considered, but are not found persuasive.

In response to Applicants submission that it would not be burdensome to search all the inventions of Claims 9-46, 48-52 and non-elected subject matter of claim 4, the Examiner recognizes that the inventions are classified differently which would necessitate different searches of the US Patents. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are

involved in the examination of each group. Moreover, with regards to Applicants contention that the process of making are not materially different from the product made, the Examiner recognizes that in order to show 1 process of making and a product made by the process can be shown to be distinct inventions if either or both of the following can be shown: (A) that the process as claimed is not an obvious process of making the product and the process as claimed can be used to make another materially different product; or (B) that the product as claimed can be made by another * materially different process (MPEP 806.05 (f)). In the instant case, the process as claimed can be used to make another materially different product such as contacting a liposome with an effective portion of RalB1, wherein RalBP1 is an antibody including IgG's which comprises 2 heavy and 2 light chains containing constant and variable regions, and includes framework regions which act as a scaffold for the 6 complementarily determining regions (CDR) that function to bind an epitope or RalBP1 is a peptide which is a single chain molecule.

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-52 are currently pending

Claims 9-46 and 48-52 have been withdrawn from consideration as being drawn to non-elected inventions.

Claims 1-8 and 47 are currently under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 10/17/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 1 and 47 have been amended to recite "an effective portion of RalBP1" instead of "an effective portion of RLIP76" as originally filed. While it is known that RalBP1 and RLIP76 are

synonyms for each other (*see iHOP database attached*), the Examiner suggests that the specification be amended to correctly identify what applicants are now claiming.

Claim Objections

Claim 4 is objected to because of the following informalities: In the instant case, Claim 4 is drawn to a non-elected inventions such as bioreactor, soil, water, spill, process waste stream, manufacturing waste, chemical waste, hospital waste and combination thereof. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 5, 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "reside" in claim 4 is a relative term which renders the claim indefinite. The term "reside" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instant case, it is unclear how to interpret the term reside in the context of where the toxic compounds are located. For example, Merriam-Webster Online Dictionary defines the term "resides" as being to dwell permanently or continuously (see attached). Thus, the claims appear to be suggesting that toxic compounds are permanently or continuously located in an organism, mammalian cell or transfected mammalian cell.

Claims 5, 6 and 7 recites the limitation "wherein adding" in claim 1. However, there does not appear to be sufficient antecedent basis for this limitation in the claim. For example, claim 1 does not appear to recite adding the proteoliposome to the toxic compound.

The phrase "wherein adding the proteoliposome to the toxic compounds reduces the concentration of toxic compounds" in claim 5 is a relative phrase which renders the claim indefinite. The phrase "wherein adding the proteoliposome to the toxic compounds reduces the concentration

of toxic compounds" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, it is unclear how the addition of a proteoliposome reduces the concentration of the toxic compound. For examination purposes, the claim will be interpreted as the addition of a solution of proteoliposome to a solution of toxic compound at a set concentration reduces the final concentration of the toxic compound.

The phrase "wherein adding the proteoliposome to the compounds protects against further contamination with one or more toxic compounds" in claim 6 is a relative phrase which renders the claim indefinite. The phrase "wherein adding the proteoliposome to the compounds protects against further contamination with one or more toxic compounds" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, it is unclear whether the addition of a proteoliposome to the compounds protects against the same compound or different compounds. For examination purposes, the claim will be interpreted as protecting from the same compound.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Claims 1 and 47 have been amended to recite a method of preparing a proteoliposome comprising the step of: contacting a liposome with an effective portion of RalBP1 to create a proteoliposome that delivers the effective amount of RalBP1 for transport of toxic compounds without the assistance of a co-transport molecule. However, a careful review of the specification as originally filed does not appear to have support for the limitation "that delivers the effective amount

of RalBP1 for transport of toxic compounds without the assistance of a co-transport molecule." While the specification appears to contemplate the use of the proteoliposome consisting of an effective portion of RalBP1 for the transport of toxic compounds, a careful review of the specification as originally filed does not appear to have support for the limitation of delivering the effective portion of RalBP1 for transport. Applicant is invited to point to clear support or specific examples of the claimed limitation in the specification as-filed or remove such amendatory language in response to this action.

Claims 1-8 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of proteoliposomes consisting of a liposome and an effective portion of RalBP1. However, the written description in this case only sets forth a proteoliposome consisting of a liposome and recombinant RalPB1 consisting of the amino acid sequence of SEQ ID NO: 2 or two primary fragments of RalBP1, e.g., C-RLIP76$^{410-654}$ and N-RLIP$^{1-367}$.

The specification teaches (page 8, paragraph 0024) that an effective portion of RLIP76 includes, but is not limited to, any combination of proteolytic peptide products that, when combined, promotes the transport or prevents the accumulation of toxic organic compounds and/or enhances resistance to the toxic compound or recombinant RLIP76. With regards to RLIP76, the specification teaches (page 16, paragraph 0047) that the primary structure of RLIP76 may be divided into 4 regions, wherein the two central regions carry a Rac1/CDC42 GAP activity and a Ral binding domain and the two flaking domain are unknown. The specification further teaches (page 16, paragraph 0047) that the peptide fragments of RLIP76 individually or in association with other fragments may catalyze various functions. However, the written description only reasonably conveys a proteoliposome consisting of a liposome and recombinant RalPB1 consisting of the amino acid sequence of SEQ ID NO: 2 or two primary fragments of RalBP1, e.g., C-RLIP76$^{410-654}$ and N-RLIP$^{1-367}$ in association with transport of a toxic compound. A description of a genus may be achieved by means of a recitation of a representative number of species falling

within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of proteolipsomes consisting of a liposome and an effective portion of RalBP1 that encompass the genus of proteolipsomes that transport toxic compounds without the assistance of a co-transport nor does it provide a description of structural features that are common to the proteolipsomes. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of a proteoliposome consisting of a liposome and recombinant RLIP76 or two primary fragments of RalBP1, e.g., C-RLIP76$^{410\text{-}654}$ and N-RLIP$^{1\text{-}367}$ is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of proteolipsomes, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25

USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a proteoliposome consisting of a liposome and recombinant RalPB1 consisting of the amino acid sequence of SEQ ID NO: 2 or two primary fragments of RalBP1, e.g., C-RLIP76$^{410\text{-}654}$ and N-RLIP$^{1\text{-}367}$, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-8 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Awasthi et al. (Biochemistry 2001; 40: 4159-4168, IDS).

Awasthi et al. teach a method of preparing a proteoliposome comprising the step of contacting a liposome with an effective portion of RalBP1 to create a proteoliposome for the transport of toxic compounds (page 4161, 1st column, Functinal Reconstitution in Proteoliposomes). With regards to the liposome, the reference teaches (page 4161, line 7) that the lipsome is asolectin, e.g. soybean phospholipids. In addition, the reference discloses (page 4160, 1st column, line 1) that RLIP76 transport is ATP dependent. Awasthi et al. also teach (page 4161, 2nd column, Transport Studies) that the method further comprises adding the proteoliposome to one or more toxic compounds such as Doxorubicin or Colchicine. For example, the reference teaches (page 4161, 2nd column, Transport Studies) that the proteoliposome in a transport buffer was added to a specific

concentration of either Doxorubicin or Colchicine. Thus, in view of the rejection above, it appears that the combination of two solutions would reduce the "final" concentration of the toxic compound; and therefore, meets the instantly claimed limitation. Moreover, while Awasthi et al. do not explicitly teach that the transport of the toxic compounds by the proteoliposome occurs without the assistance of a co-transport molecule, the claimed functional limitation would be an inherent property of the proteoliposome since the specification teaches (page 13, paragraph 0042) that RLIP76 transport does not require GSH co-transport. Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). Furthermore, although Awasthi et al. do not specifically teach that the addition of the proteoliposome protects against further accumulation of the toxic compound and/or prevents the accumulation of toxic compounds, the functional limitation would be an inherent property of the referenced method because as evidenced by Awasthi et al. (Toxicol. Applied Pharm. 1999; 155: 215-226), a transporter such as DNP-SG ATPase (RLIP76) can act as a mechanism for reducing colfhicine accumulation in cells (page 223, 2nd column, 2nd paragraph). Thus, the claimed proteoliposome appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Hence, even though the claims are drawn to a mechanism by which the addition of the proteoliposome to a toxic compound protects and or prevents the accumulation of toxic compounds, the claimed method does not appear to distinguish over the prior art teaching of the same or nearly the same method. The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but

inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
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PRIMARY EXAMINER